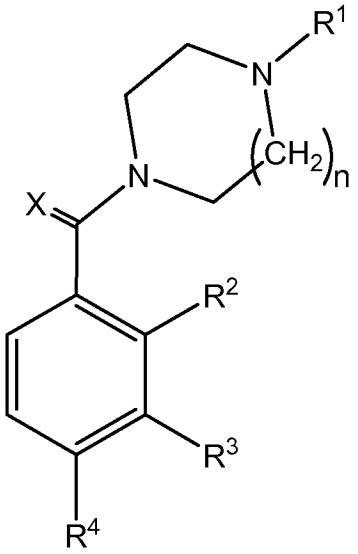
In the Claims:

This listing of claims will replace all prior versions and listing of claims in this application.

1. (currently amended) A ~~a~~ compound of formula **(I):**



(I)

wherein

R^1 is C_{1-10} alkyl, C_{3-8} alkenyl, C_{3-8} cycloalkyl, (C_{3-8} cycloalkyl)C_{1-6} alkyl, (C_{3-8} cycloalkyl)C_{3-8} alkenyl, or (C_{1-8} alkylcarbonyl)C_{1-8} alkyl;

n is 1;

X is O ~~or S~~;

~~one of~~ R^2~~,~~ and R^3 ~~and R^4 is G and the other two~~ independently are hydrogen, fluoro, chloro, bromo, nitro, trifluoromethyl, methyl, or C_{1-3}alkoxy;

R^4 is G

G is LQ;

L is ~~unbranched $(CH_2)_m$ wherein m is an integer from 1 to 7~~ $-CH_2-$;

~~Q is NR^8R^9 wherein R^8 is independently selected from hydrogen, C_{1-6} alkyl, C_{3-6} alkenyl, 3-9 membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (6-9 membered heterocyclyl)C_{1-6} alkylene, and (phenyl)C_{1-6} alkylene; and R^9 is independently selected from C_{1-6} alkyl, C_{3-6} alkenyl, 6-9 membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (6-9 membered heterocyclyl)C_{1-6} alkylene, and (phenyl)C_{1-6} alkylene; or~~

Q is a saturated, un-substituted ~~3-12 membered~~ N-linked heterocyclyl, selected from the group consisting of diazepanyl, azepanyl, morpholinyl, decahydroisoquinolin-2-yl, piperidinyl and pyrrolidinyl;

~~wherein, in addition to the N-linking nitrogen, the 3-12 membered heterocyclyl may optionally contain between 1 and 3 additional heteroatoms independently selected from O, S, and NH;~~

~~wherein Q is optionally substituted with 1-3 substituents independently selected from the group consisting of hydroxy, halo, carboxamide, C_{1-6} alkyl, 5-9 membered or 6-9 membered heterocyclyl, $N(C_{1-6}$ alkyl)(5-9 membered or 6-9 membered heterocyclyl), NH(5-9 membered or 6-9 membered heterocyclyl), O(5-9 or 6-9 membered heterocyclyl), (5-9 membered or 6-9 membered heterocyclyl)C_{1-3} alkylene, C_{1-6} alkoxy, (C_{3-6} cycloalkyl)-O-, phenyl, (phenyl)C_{1-3} alkylene, and (phenyl)C_{1-3} alkylene-O-, where each of above heterocyclyl, phenyl, and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, methoxy, halo, nitro, cyano, hydroxy, and C_{1-3} alkyl;~~

provided however that when R^1 is methyl, G is not piperidin-1-ylmethyl; and

wherein each of the above alkyl, ~~alkylene,~~ alkenyl, ~~heterocyclyl,~~ and cycloalkyl, ~~carbocyclyl, and aryl~~ groups may each be independently and optionally substituted with between 1 and 3 substituents independently selected from trifluoromethyl, methoxy, halo, amino, nitro, hydroxy, and C_{1-3} alkyl;

~~provided that when R^1 is methyl or ethyl, R^2 and R^3 are both H and X is O, then R^4 is not [[5-chloro-1-(1,1-dimethylethyl)-1,6-dihydro-6-oxo-4-pyridazinyl]amino]methyl; and~~

provided that when R^1 is methyl, R^2 and R^3 are both H and X is O, then R^4 is not 4-morpholin-4-ylmethyl;

or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.

2. (original) A compound of claim 1, wherein R^1 is C_{1-10} alkyl.

3. (original) A compound of claim 1, wherein R^1 is C_{3-5} alkyl.

4. (original) A compound of claim 1, wherein wherein R^1 is isopropyl.

5-21: Cancelled

22. (currently amended) A compound of claim 56, wherein R^9 is C_{1-6} alkyl.

23. (currently amended) A compound of claim 56, wherein R^9 is unsubstituted or substituted phenyl.

24. Cancelled

25. (currently amended) A compound of claim 57, wherein R^8 and R^9 are methyl.

26. (currently amended) A compound of claim 57, wherein R^8 and R^9 are ethyl.

27. (currently amended) A compound of claim 56, wherein R^9 is selected from phenyl or 5-9 membered aromatic heterocyclyl, wherein said phenyl or aromatic heterocyclyl is optionally substituted with 1-3 substituents selected from methoxy, hydroxy, halo, nitro, amino, trifluoromethyl, and C_{1-3} alkyl.

28. (previously presented) A compound of claim 27, wherein R^9 is selected from substituted or unsubstituted phenyl, pyridyl, pyrimidyl, furyl, thiofuryl, imidazolyl, (imidazolyl)C_{1-3} alkylene, oxazolyl, thiazolyl, 2,3-dihydro-indolyl, benzimidazolyl, 2-oxobenzimidazolyl, (tetrazolyl)C_{1-3} alkylene, tetrazolyl, (triazolyl)C_{1-3} alkylene, triazolyl, (pyrrolyl)C_{1-3} alkylene, pyrrolidinyl, and pyrrolyl.

29. (original) A compound of claim 28, wherein R^9 is phenyl.

30. (original) A compound of claim 28, wherein R^9 is substituted or unsubstituted pyridyl.

Claims 31-40: Cancelled

41. (original) A compound of claim 1 selected from the group consisting of:
(4-Azepan-1-ylmethyl-phenyl)-(4-*sec*-butyl-piperazin-1-yl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;

(4-*sec*-Butyl-piperazin-1-yl)-(4-piperidin-1-ylmethyl-phenyl)-methanone;
{4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-piperidin-1-ylmethyl-phenyl)-methanone;
{4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-pyrrolidin-1-ylmethyl-phenyl)-methanone;
(4-Isopropyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone;
(4-sec-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride; and
{4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride.

42. (original) A pharmaceutical composition, comprising a compound of claim 1 and a pharmaceutically-acceptable excipient.

43. (original) A compound of claim 1 isotopically-labelled to be detectable by PET or SPECT.

Claims 44-46: Cancelled

47. (withdrawn) A method for treating a disease or condition modulated by at least one receptor selected from the histamine H_1 receptor and the histamine H_3 receptor, said method comprising (a) administering to a subject a jointly effective amount of a histamine H_1 receptor antagonist compound, and (b) administering to the subject a jointly effective amount of a compound of claim 1, said method providing a jointly therapeutically effective amount of said compounds.

48. (withdrawn) The method of claim 47 wherein the histamine H_1 receptor antagonist and the compound of claim 1 are present in the same dosage form.

49. (withdrawn) A method for treating diseases or conditions modulated by at least one receptor selected from the histamine H_2 receptor and the histamine H_3 receptor in a subject, comprising (a) administering to the subject a jointly effective amount of a histamine H_2 receptor antagonist compound, and (b) administering to the subject a jointly effective amount of a compound of claim 1, said method providing a jointly therapeutically effective amount of said compounds.

50. (withdrawn) The method of claim 39 wherein the histamine H_2 receptor antagonist and the compound of claim 1 are present in the same dosage form.

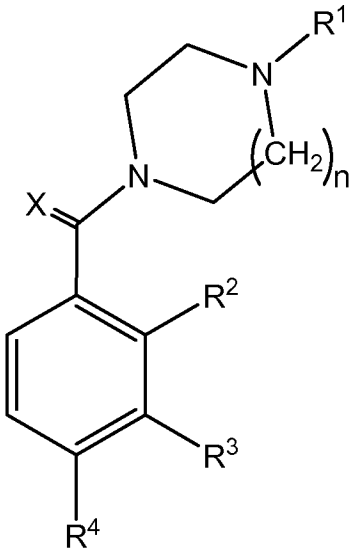
51. (original) A method for treating one or more disorders or conditions selected from the group consisting of sleep/wake disorders, narcolepsy, and arousal/vigilance disorders, comprising administering to a subject a therapeutically effective amount of a compound of claim 1.

52. (original) A method for treating attention deficit hyperactivity disorders (ADHD), comprising administering to a subject a therapeutically effective amount of a compound of claim 1.

53. (original) A method for treating one or more disorders or conditions selected from the group consisting of dementia, mild cognitive impairment (pre-dementia), cognitive dysfunction, schizophrenia, depression, manic disorders, bipolar disorders, and learning and memory disorders, comprising administering to a subject a therapeutically effective amount of a compound of claim 1.

Claims 54 and 55: Cancelled

56. (new) A compound of formula **(I):**



(I)

wherein

R^1 is C_{1-10} alkyl, C_{3-8} alkenyl, C_{3-8} cycloalkyl, (C_{3-8} cycloalkyl)C_{1-6} alkyl, (C_{3-8} cycloalkyl)C_{3-8} alkenyl, or (C_{1-8} alkylcarbonyl)C_{1-8} alkyl;

n is 1;

X is O or S;

one of R^2, R^3 and R^4 is G and the other two independently are hydrogen, fluoro, chloro, bromo, nitro, trifluoromethyl, methyl, or C_{1-3}alkoxy;

G is LQ;

L is unbranched $-(CH_2)_m-$ wherein m is an integer from 1 to 7;

Q is NR^8R^9 wherein R^8 is hydrogen; and R^9 is independently selected from C_{1-6} alkyl, C_{3-6} alkenyl, 6-9 membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (6-9-membered heterocyclyl)C_{1-6} alkylene, and (phenyl)C_{1-6} alkylene; or

Q is a saturated 3-12 membered N-linked heterocyclyl, wherein, in addition to the N-linking nitrogen, the 3-12 membered heterocyclyl may optionally contain between 1 and 3 additional heteroatoms independently selected from O, S, and NH;

wherein Q is optionally substituted with 1-3 substituents independently selected from the group consisting of hydroxy, halo, carboxamide, C_{1-6} alkyl, 5-9 membered or 6-9 membered heterocyclyl, -N(C_{1-6} alkyl)(5-9 membered or 6-9 membered heterocyclyl), -NH(5-9 membered or 6-9 membered heterocyclyl), -O(5-9 or 6-9 membered heterocyclyl), (5-9 membered or 6-9 membered heterocyclyl)C_{1-3} alkylene, C_{1-6} alkoxy, (C_{3-6} cycloalkyl)-O-, phenyl, (phenyl)C_{1-3} alkylene, and (phenyl)C_{1-3} alkylene-O-, where each of above heterocyclyl, phenyl, and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, methoxy, halo, nitro, cyano, hydroxy, and C_{1-3} alkyl;

provided however that when R^1 is methyl, G is not piperidin-1-ylmethyl; and

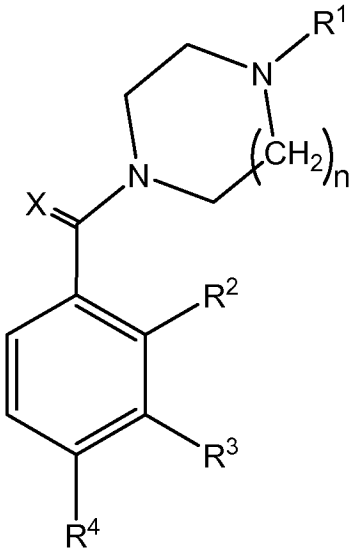
wherein each of the above alkyl, alkylene, alkenyl, heterocyclyl, cycloalkyl, carbocyclyl, and aryl groups may each be independently and optionally substituted with between 1 and 3 substituents independently selected from trifluoromethyl, methoxy, halo, amino, nitro, hydroxy, and C_{1-3} alkyl;

provided that when R^1 is methyl or ethyl, R^2 and R^3 are both H and X is O, then R^4 is not [[5-chloro-1-(1,1-dimethylethyl)-1,6-dihydro-6-oxo-4-pyridazinyl]amino]methyl; and

provided that when R^1 is methyl, R^2 and R^3 are both H and X is O, the R^4 is not 4-morpholin-4-ylmethyl;

or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.

57. (new) A compound of formula **(I):**



(I)

wherein

R^1 is C_{1-10} alkyl, C_{3-8} alkenyl, C_{3-8} cycloalkyl, (C_{3-8} cycloalkyl)C_{1-6} alkyl, (C_{3-8} cycloalkyl)C_{3-8} alkenyl, or (C_{1-8} alkylcarbonyl)C_{1-8} alkyl;

n is 1;

X is O or S;

one of R^2, R^3 and R^4 is G and the other two independently are hydrogen, fluoro, chloro, bromo, nitro, trifluoromethyl, methyl, or C_{1-3}alkoxy;

G is LQ;

L is unbranched $–(CH_2)_m–$ wherein m is an integer from 1 to 7;

Q is NR^8R^9 wherein R^8 and R^9 are independently selected from C_{1-6} alkyl; or

Q is a saturated 3-12 membered N-linked heterocyclyl, wherein, in addition to the N-linking nitrogen, the 3-12 membered heterocyclyl may optionally contain between 1 and 3 additional heteroatoms independently selected from O, S, and NH;

wherein Q is optionally substituted with 1-3 substituents independently selected from the group consisting of hydroxy, halo, carboxamide, C_{1-6} alkyl, 5-9 membered or 6-9 membered heterocyclyl, -N(C_{1-6} alkyl)(5-9 membered or 6-9 membered heterocyclyl), -NH(5-9 membered or 6-9 membered heterocyclyl), -O(5-9 or 6-9

membered heterocyclyl), (5-9 membered or 6-9 membered heterocyclyl)C_{1-3} alkylene, C_{1-6} alkoxy, (C_{3-6} cycloalkyl)-O-, phenyl, (phenyl)C_{1-3} alkylene, and (phenyl)C_{1-3} alkylene-O-, where each of above heterocyclyl, phenyl, and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, methoxy, halo, nitro, cyano, hydroxy, and C_{1-3} alkyl;

provided however that when R^1 is methyl, G is not piperidin-1-ylmethyl; and

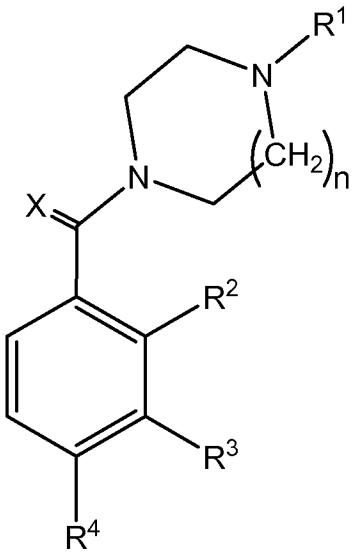
wherein each of the above alkyl, alkylene, alkenyl, heterocyclyl, cycloalkyl, carbocyclyl, and aryl groups may each be independently and optionally substituted with between 1 and 3 substituents independently selected from trifluoromethyl, methoxy, halo, amino, nitro, hydroxy, and C_{1-3} alkyl;

provided that when R^1 is methyl or ethyl, R^2 and R^3 are both H and X is O, then R^4 is not [[5-chloro-1-(1,1-dimethylethyl)-1,6-dihydro-6-oxo-4-pyridazinyl]amino]methyl; and

provided that when R^1 is methyl, R^2 and R^3 are both H and X is O, the R^4 is not 4-morpholin-4-ylmethyl;

or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.

58. (new) A compound of formula **(I):**



(I)

wherein

R^1 is C_{1-10} alkyl, C_{3-8} alkenyl, C_{3-8} cycloalkyl, (C_{3-8} cycloalkyl)C_{1-6} alkyl, (C_{3-8} cycloalkyl)C_{3-8} alkenyl, or (C_{1-8} alkylcarbonyl)C_{1-8} alkyl;

n is 1;

X is O or S;

one of R^2, R^3 and R^4 is G and the other two independently are hydrogen, fluoro, chloro, bromo, nitro, trifluoromethyl, methyl, or C_{1-3}alkoxy;

G is LQ;

L is $–CH_2CH_2–$;

Q is NR^8R^9 wherein R^8 is independently selected from hydrogen, C_{1-6} alkyl, C_{3-6} alkenyl, 3-9 membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (6-9-membered heterocyclyl)C_{1-6} alkylene, and (phenyl)C_{1-6} alkylene; and R^9 is independently selected from C_{1-6} alkyl, C_{3-6} alkenyl, 6-9 membered carbocyclyl, 3-12 membered heterocyclyl, phenyl, (6-9-membered heterocyclyl)C_{1-6} alkylene, and (phenyl)C_{1-6} alkylene; or

Q is a saturated 3-12 membered N-linked heterocyclyl, wherein, in addition to the N-linking nitrogen, the 3-12 membered heterocyclyl may optionally contain between 1 and 3 additional heteroatoms independently selected from O, S, and NH;

wherein Q is optionally substituted with 1-3 substituents independently selected from the group consisting of hydroxy, halo, carboxamide, C_{1-6} alkyl, 5-9 membered or 6-9 membered heterocyclyl, -N(C_{1-6} alkyl)(5-9 membered or 6-9 membered heterocyclyl), -NH(5-9 membered or 6-9 membered heterocyclyl), -O(5-9 or 6-9 membered heterocyclyl), (5-9 membered or 6-9 membered heterocyclyl)C_{1-3} alkylene, C_{1-6} alkoxy, (C_{3-6} cycloalkyl)-O-, phenyl, (phenyl)C_{1-3} alkylene, and (phenyl)C_{1-3} alkylene-O-, where each of above heterocyclyl, phenyl, and alkyl groups may be optionally substituted with from 1 to 3 substituents independently selected from trifluoromethyl, methoxy, halo, nitro, cyano, hydroxy, and C_{1-3} alkyl;

provided however that when R^1 is methyl, G is not piperidin-1-ylmethyl; and

wherein each of the above alkyl, alkylene, alkenyl, heterocyclyl, cycloalkyl, carbocyclyl, and aryl groups may each be independently and optionally substituted with between 1 and 3 substituents independently selected from trifluoromethyl, methoxy, halo, amino, nitro, hydroxy, and C_{1-3} alkyl;

provided that when R^1 is methyl or ethyl, R^2 and R^3 are both H and X is O, then R^4 is not [[5-chloro-1-(1,1-dimethylethyl)-1,6-dihydro-6-oxo-4-pyridazinyl]amino]methyl; and

provided that when R^1 is methyl, R^2 and R^3 are both H and X is O, the R^4 is not 4-morpholin-4-ylmethyl;

or a pharmaceutically acceptable salt, ester, tautomer, solvate or amide thereof.

59. (new) Acompound of claim 1, wherein R^1 is C_{3-8} cycloalkyl.

60. (new) A compound that is: Isopropyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone.

61. (new) A compound that is: (4-sec-Butyl-piperazin-1-yl)-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride.

62. (new) A compound that is: {4-(1-Ethyl-propyl)-piperazin-1-yl}-(4-morpholin-4-ylmethyl-phenyl)-methanone dihydrochloride.